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 **What is implantation?**

Implantation, in reproduction physiology, the adherence of a fertilized egg to a surface in the reproductive tract, usually to the uterine wall (see uterus), so that the egg may have a suitable environment for growth and development into a new offspring. Fertilization of the egg usually occurs after the egg has left the ovary and is being transported through the fallopian tubes. Male sperm cells deposited in the female reproductive tract travel up to the fallopian tubes to unite with the egg. Once fertilized, the egg begins to undergo a series of cell divisions. The egg takes up to seven days to reach the uterus; by this time the single-celled egg has divided numerous times, so that it is a ball of approximately 200 cells.

The uterus has thick walls suitable for egg attachment and growth. A female hormone known as progesterone, secreted by the corpus luteum in the ovary, influences the readiness of the uterine wall for egg implantation. It increases the blood supply in the wall, water content, and secretion of glycogen, a nutrient for the surrounding tissue and developing egg. If the uterus is not first prepared by progesterone, the egg will not attach itself. Progesterone also inhibits muscular contractions in the uterine wall that would tend to reject the adhering egg.

When the egg reaches the uterus, it usually remains free in the uterine cavity for about a day. It then attaches to the uterine lining (the endometrium). Cells in the outer surface of the egg grow rapidly once contact is made with the uterine wall. The egg disrupts the surface of the endometrium and actively burrows into the deeper tissue. By the 11th day after fertilization, the egg has completely embedded itself into the endometrium. The product of conception—first the fertilized egg and then the developing child and the placenta—normally remains implanted in the human uterus for nine months

Implantation is the attachment of a fertilized egg to the wall of the uterus and typically occurs between 6 and 12 days after ovulation, with most cases happening around day 9. At the point where the fertilized egg enters the uterus, it’s known as a blastocyst — a round collection of stem cells in a fluid with an outer layer that eventually forms the placenta. This outer layer is essential in this process because it is what adheres to and merges with the endometrium or uterine lining.

**Diagram on implantation**

**What is implantation during pregnancy?**

Implantation is the window of time during early pregnancy when a cluster of rapidly dividing cells — called a blastocyst — makes its way down the fallopian tube and burrows deep into the lining of the uterus. There, the newly hatched embryo starts releasing hormones that prepare your body for baby, turning off your period, building up the placenta, and possibly making you feel crampy and tired.

**When does implantation occur?**

Implantation is often described as a window because it occurs about 8 to 9 days after fertilization, though it can happen as early as 6 days and as late as 12 days after ovulation. While many consider fertilization to be the start of pregnancy, successful implantation is the more crucial hurdle.

What is the endometrium, and what does the endometrium do?

The uterine lining -- also known as the endometrium -- is composed of two layers:

The basal layer never sheds. It is the part of the endometrium that helps form the other layer.

The functional layer builds up after the previous menstrual cycle ends, forming a perfect environment for a fertilized egg. If the egg is not fertilized, the functional layer will shed during the next menstrual cycle.

When an egg is fertilized, it implants in the uterine lining. This usually occurs between 6 and 12 days after ovulation and about 5 to 6 days after fertilization.

Once implanted, the embryo secretes hormones, including human chorionic gonadotropin (hCG), which signals to the mother’s body that she is pregnant. This halts the menstrual cycle and prevents the functional layer of the endometrium from being shed.

From this point on, the uterine lining will turn into the placenta, which provides oxygen and nutrients to the baby.

Even when there’s no implanted egg to sustain, the uterine lining serves a critical function. The endometrium prevents adhesions of the underlying myometrium layer, which contains the muscle tissue that causes contractions. If adhesions form, it’s possible for the uterus to collapse, preventing normal menstruation and pregnancy.

**What role does the endometrium play in implantation?**

Studies show that cycles with thicker uterine linings result in successful pregnancies more often. In most successful implantations, the arrival of the egg coincides with peak levels of luteinizing hormone (LH), which primes the endometrium to accept the embryo.

In addition to LH, a chemical called trypsin, produced by the embryo signals the uterine lining to prepare for implantation. A favorable endometrium is thick and exhibits a triple-line pattern under ultrasound imaging.

Unfortunately, even if an egg is successfully fertilized, it is possible for the embryo to fail to implant in the uterine lining. In two out of three cases, this is due to inadequate uterine receptivity. Many factors can contribute to uterine receptivity, including hormones and a type of proteins called cytokines, which allow cells to send and receive signals. Some medications, including progestins and progesterone, can increase the chances of successful implantation after repeated failure.

**What can cause implantation to fail?**

Unfortunately, various conditions can hamper the proper implantation of a blastocyst. In some cases, genetic disorders in the developing embryo disrupt the trypsin signal and cause a stress reaction that forces the uterus to reject the blastocyst. Immunological disorders may cause the mother’s body to attack the implanting embryo. Ultimately, this is a delicate process, and roughly half of all fertilized eggs fail to successfully implant.

**Signs of Successful Implantation**

If the embryo successfully implants, you can expect to experience a number of signs or symptoms. Unfortunately, the earliest signs of success can appear like the normal signs of a period: cramps, headaches, fatigue, and bloating. In 20% to 30% of women, implantation bleeding occurs, similar to what they experience during a period.

However, if it's implantation and not your period, additional symptoms will follow:

Your breasts may feel sore, tight, or tender.

If you continue tracking your basal body temperature after ovulation, you may notice that your average temperature has increased.

This rise in temperature, combined with fatigue and other symptoms, may make you think you have the flu.

Within a week, you may feel more frequent urges to urinate. This is because increased blood flow to the uterus has put pressure on your bladder.

What is implantation bleeding and how can I tell the difference between that and my period?

The difference between implantation symptoms and your period can be confusing. If implantation causes bleeding, chances are it will be light and spotty, and will happen before your period is scheduled to arrive. These symptoms should be minor and are nothing to worry about.

Approximately 15 to 25 percent of women experience light bleeding as a result of implantation. Blood flows when cells shed from the oxygen-rich tissue that lines your uterus during the process. Implantation bleeding will appear days before you expect your menstrual cycle to start, and, compared to your period, will be scant and spotty, starting out pink and turning brown. Unlike your period, it probably won't flow or contain clots, and should stop within a day or two.

**Stages of implantation:**

Implantation consist of three stages:

(a) the blastocyst contacts the implantation site of the endometrium (apposition)

(b) trophoblast cells of the blastocyst attach to the receptive endometrial epithelium (adhesion)

(c) invasive trophoblast cells cross the endometrial epithelial basement membrane and invade the endometrial stroma

1. Implantation begins with apposition of the blastocyst at the uterine epithelium, generally about 2-4 days after the morula enters the uterine cavity. The implantation site in the human uterus is usually in the upper and posterior wall in the mid sagittal plane. Implantation is considered a pro-inflammatory reaction in which endometrial vascular permeability is markedly increased at the attachment site, mediated by Cyclooxygenase (Cox)-derived prostaglandins. Prostaglandin E2 is increased in the luminal epithelium and the underlying stroma at the both of mice and human implantation site, thus indicating its role in attachment and localized endometrial vascular permeability. Prostaglandin E2 is considered as one of the important regulators of human trophoblast invasion, which activates other signaling proteins . During apposition process, the blastocyst differentiates into an inner cell mass (embryo) and trophectoderm (placenta). Stromal cells surrounding the implanting blastocyst differentiate into a specialized cell type called decidual cells, via a process known as decidualization.

Cytokines are regulatory peptides or glycoproteins. Unlike hormones, cytokines usually act as paracrine or autocrine signals in local tissue, and only occasionally, they have more distant effects as endocrine mediators.

2. Cell adhesion of the blastocyst trophectoderm and endometrial luminal epithelial cells of the uterus is mediated by cell adhesion molecules, including integrins, cadherins, selectins, and immunoglobulins. Cell adhesion molecules are expressed on the surface of invasive trophoblast, and these molecules interact with ligands expressed by the extra-cellular matrix of the decidua in a temporal and spatial way . Integrins are a family of transmembrane glycoproteins that act as cell surface receptors formed by various combinations of two different, non-covalently linked α and β subunits. Menstrual cycle-specific integrins are up-regulated in the mid-luteal phase of human endometrium and have been considered as markers of the window of implantation. It has been suggested that a lack of integrin expression during the window of implantation can contribute to unexplained infertile women . HThe trophoblast also expresses integrins at the time of implantation and at a site of outgrowing trophoblast cells . Cadherins are a family of glycoproteins involved in the Ca2+-dependent cell-cell adhesion mechanism .

3. Invasion

The process of implantation allows fetal trophoblast cells to invade and migrate into the maternal decidua. By this time, the trophoblasts at the implantation site have formed masses of cytotrophoblasts and syncytiotrophoblasts. Eventually, trophoblast cells destroy the wall of the maternal spiral arteries, converting them from muscular vessels into flaccid sinusoidal sacs lined with endovascular trophoblast . The aim of invasion is to reconstruct the maternal spiral arteries, which will maintain a high blood flow between the fetus and the mother, replacing small, high-resistance vessels with large, low-resistance vessels. The extent of trophoblastic invasion determines later placental efficiency and fetal viability in late gestation. Deficiencies in trophoblastic invasion give rise to adverse pregnancy outcomes such as intrauterine growth restriction (IUGR) and preeclampsia . Formation of placental villi is associated with remodeling of the extra-cellular matrix through tissue degradation and revision by various proteinases including serine proteases, matrix metalloproteinases (MMPs) and collagenases . Serine proteases, including urokinase-type plasminogen activator (uPA) and tissue-type plasminogen activator (tPA) can catalyze the conversion of plasminogen to plasmin for proteolytic degradation of the ECM. Trophoblast cells express plasminogen activator receptors. Invasion and migration of mouse trophoblastic cells are closely related to their PA activity . The zinc-dependent family of MMPs is a key player in matrix degradation during trophoblastic invasion. The MMP family is classified into three groups, including collagenases, gelatinases, and stromelysins based on the specificity of substrate. Type IV collagen is a fundamental component of the basal membrane and it is one of the major structures of the uterine ECM. The invasive capacity of human trophoblastic cells has been shown to correlate with increased production of type IV collagenase (MMP-2 and MMP-9).

During early pregnancy, fetal trophoblast cells invade the uterus and penetrate the basement membrane, a property that is characteristic of malignant cells. However, unlike tumor invasion, trophoblast invasion of the uterus should be under strict control confining the placenta and within the time constraint of a pregnancy. Limitation of trophoblastic invasion is attributed to the balance of activating and inhibiting growth factors, cytokines, and enzymes. Decidual cells produce plasminogen activator inhibitor-1 which is the major inhibitor of uPA . The tissue inhibitors of MMPs tightly regulate the activities of MMPs. Decidual transforming growth factor (TGF)-β plays a major regulatory role in limitation of human trophoblast invasion by up-regulating both TIMPs and PAI-1 . In addition, TGF-β provides anti proliferative signals to differentiate from invasive and proliferative cytotrophoblasts into non-invasive and multi nucleated syncytiotrophoblasts at the human fetal-maternal interface. Decorin, a decidua-derived TGF-β binding proteoglycan, negatively regulates proliferation, migration, and invasiveness of human extravillous trophoblast cells in a TGFβ-independent manner.

**Signs of implantation**

Bleeding

It’s actually a little unclear how common implantation bleeding is. Some sources claim that one-third of all women who become pregnant experience implantation bleeding, but this actually isn’t backed by peer-reviewed research. (Something on the internet that may not be true? Say it ain’t so!)

Here’s what we can tell you. Up to 25 percent of women experience bleeding or spotting in the first trimester — and implantation is one cause of first trimester bleeding.

This bleeding can be confusing, because it may happen around the time that your regular period would start. Most commonly though, it will occur a few days to a week before you expect your menstrual period.

There are other differences that can help you determine whether you are experiencing implantation bleeding or your period:

implantation bleeding is most likely to be light pink or brown (as opposed to the bright or dark red of your period)

implantation bleeding is more like spotting than an actual flow of blood

This spotting may occur once, or last for a few hours, or even up to three days. You may notice some pink or brown discharge when you wipe or on your underwear, but you won’t need a full pad or tampon — possibly not for many months!

Cramps

It’s no secret that early pregnancy causes a rapid shift of hormones. More specifically, implantation is a trigger for the hormone surge — that’s why you can’t get that second pink line on a home pregnancy test until after implantation.

And the changing hormonal tide can also cause cramping. Furthermore, there’s a lot going on in your uterus as the fertilized egg implants and begins to grow.

While there’s no research indicating that implantation itself causes cramps, some women do feel abdominal tenderness, lower back pain, or cramping around the time of implantation. This may seem like a mild version of how you feel before your period starts.

Discharge

Let’s talk about what’s going on down there.

If you’ve been monitoring your cervical mucus, good work, future mama! Being aware of what’s going on with your body can be empowering when trying to conceive.

You may notice some cervical mucus changes around the time of implantation.

During ovulation, your cervical mucus will be clear, stretchy, and slippery (sort of like egg whites). You probably already know this as your green light to get your baby dance on.

After implantation occurs, your mucus might have a thicker, “gummier” texture and be clear or white in color.

And in the days of early pregnancy, rising progesterone and estrogen may cause your mucus to become even thicker, more profuse, and white or yellow in color.

We hate to say it, though: Cervical mucus can be affected by a number of things (hormones, stress, intercourse, pregnancy, implantation bleeding or your period, etc.) and may not be a reliable indicator of whether or not implantation has occurred.

Start tracking your cervical mucus while you’re not pregnant, and a more useful indicator may be how different it is from your norm during each stage of your cycle.

Bloating

Rising progesterone (which happens in early pregnancy) slows your digestive system down. This can make you feel bloated. But as so many of us know, this feeling can be a really common symptom of your period, too. Want to know why? Progesterone also rises when your period is imminent. Thanks, hormones.

Tender breasts

After implantation, levels of hCG, estrogen, and progesterone all increase rapidly. This can cause your boobs to feel very sore. (These hormones sure are multitaskers!) While many women experience breast swelling or tenderness before their periods, this is likely to be more noticeable than usual in very early pregnancy.

Nausea

Ah, arguably the most famous of the early pregnancy symptoms: nausea, aka “morning sickness” (though it can happen at any time of day).

Increased levels of progesterone following implantation can make you feel nauseous. But again, this most commonly occurs around 4 or 5 weeks of pregnancy (about the time you miss your period).

Progesterone slows down your digestion, which can contribute to nausea. Rising hCG levels and a more sensitive sense of smell can make the problem worse — so now might be a good time to avoid cooking liver and onions.

Headache rising hormone levels (particularly progesterone) can also give you headaches following implantation.

Mood swings

Find yourself content and happy one minute, and weeping at a commercial on TV the next? Or excited to see your partner in the evening and then biting their head off over nothing? You may be experiencing mood swings.

Estrogen and progesterone, as well as hCG, increase very quickly following implantation. This can make you feel “off” or moodier than usual.

Implantation dip

While this sounds like some kind of weird appetizer, “implantation dip” refers to a one-day decrease in your basal body temperature that can occur as a result of implantation.

If you’ve been tracking your basal body temperature (BBT) to help identify your most fertile days, you likely already have a log of your daily BBT over the course of a few months.

Typically, a woman’s temperature is lower before ovulation, and then increases, and then drops again before her period starts. If you get pregnant, your temperature remains elevated.

Some women seem to experience a one-day drop in temperature around the time of implantation. This is different than the drop in temperature that means your period is coming — in the case of an imminent period, your temperature would stay low.